## AMENDMENT TO THE SPECIFICATION

Please insert the following paragraph and related heading as the first full paragraph on page 1.

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims the priority benefit of U.S. Provisional Patent Application No. 60/441,392 filed January 21, 2003; U.S. Provisional Patent Application No. 60/441,377 filed January 21, 2003; U.S. Provisional Patent Application No. 60/441,502 filed January 21, 2003; U.S. Provisional Patent Application No. 60/441,405 filed January 21, 2003; U.S. Provisional Patent Application No. 60/441,447 filed January 21, 2003; U.S. Provisional Patent Application No. 60/441,381 filed January 21, 2003; and U.S. Provisional Patent Application No. 60/392,415 filed June 26, 2002.

Please replace the first full paragraph on page 4 with the following amended paragraph.

The transposon-based vectors of the present invention include a transposase, operably-linked to a first promoter, and a coding sequence for a protein or peptide of interest operably-linked to a second promoter, wherein the coding sequence for the protein or peptide of interest and its operably-linked promoter are flanked by transposase insertion sequences recognized by the transposase. The transposon-based vector also includes the following characteristics: a) one or more modified Kozak sequences comprising ACCATG (SEQ ID NO:13) ~~at the~~ 3' ~~end~~ of the first promoter to enhance expression of the transposase; b) modifications of the codons for the first several N-terminal amino acids of the transposase, wherein the nucleotide at the third base position of each codon was changed to an A or a T without changing the corresponding amino acid; c) addition of one or more stop codons to enhance the termination of transposase synthesis; and/or, d) addition of an effective polyA sequence operably-linked to the transposase to further enhance expression of the transposase gene.

Please replace the paragraph that begins on page 13 and ends on page 14 with the following amended paragraph.

The transposon-based vectors of the present invention include a transposase gene operably-linked to a first promoter, and a coding sequence for a desired protein or peptide operably-linked to a second promoter, wherein the coding sequence for the desired protein or peptide and its operably-linked promoter are flanked by transposase insertion sequences recognized by the transposase. The transposon-based vector also includes one or more of the following characteristics: a) one or more modified Kozak sequences comprising ACCATG (SEQ ID NO:13) ~~at the~~ 3' ~~end~~ of the first promoter to enhance expression of the transposase; b) modifications of the codons for the first several N-terminal amino acids of the transposase, wherein the third base of each codon was changed to an A or a T without changing the corresponding amino acid; c) addition of one or more stop codons to enhance the termination of transposase synthesis; and, d) addition of an effective polyA sequence operably-linked to the transposase to further enhance expression of the transposase gene. Figure 1 shows a schematic representation of several components of the transposon-based vector. The present invention further includes vectors containing more than one gene of interest, wherein a second or subsequent gene of interest is operably-linked to the second promoter or to a different promoter. It is also to be understood that the transposon-based vectors shown in the Figures are representational of the present invention and that the order of the vector elements may be different than that shown in the Figures, that the elements may be present in various orientations, and that the vectors may contain additional elements not shown in the Figures.

Please replace the first full paragraph on page 14 with the following amended paragraph.

In a further embodiment of the present invention, the transposase found in the transposase-based vector is an altered target site (ATS) transposase and the insertion sequences are those recognized by the ATS transposase. However, the transposase located in the transposase-based vectors is not limited to a modified ATS transposase and can be derived from any transposase. Transposases known in the prior art include those

found in AC7, Tn5SEQ1, Tn916, Tn951, Tn1721, Tn 2410, Tn1681, Tn1, Tn2, Tn3, Tn4, Tn5, Tn6, Tn9, Tn10, Tn30, Tn101, Tn903, Tn501, Tn1000 (γδ), Tn1681, Tn2901, AC transposons, Mp transposons, Spm transposons, En transposons, Dotted transposons, Mu transposons, Ds transposons, dSpm transposons and I transposons. According to the present invention, these transposases and their regulatory sequences are modified for improved functioning as follows: a) the addition one or more modified Kozak sequences comprising ACCATG (SEQ ID NO:13) ~~at the~~ 3' ~~end~~ of the promoter operably-linked to the transposase; b) a change of the codons for the first several amino acids of the transposase, wherein the third base of each codon was changed to an A or a T without changing the corresponding amino acid; c) the addition of one or more stop codons to enhance the termination of transposase synthesis; and/or, d) the addition of an effective polyA sequence operably-linked to the transposase to further enhance expression of the transposase gene.

Please replace the paragraph that begins on page 27 and ends on page 28 with the following amended paragraph.

Another non-limiting list of the antibodies that may be produced using the present invention is provided in product catalogs of companies such as Phoenix Pharmaceuticals, Inc. (~~www.phoenixpeptide.com;~~ 530 Harbor Boulevard, Belmont, CA), Peninsula Labs (San Carlos CA), SIGMA[[,]] (St.Louis, MO ~~www.sigma-aldrich.com~~), Cappel ICN[[,]] (Irvine, California), ~~www.icnbiomed.com,~~ and Calbiochem[[,]] (La Jolla, California), ~~www.calbiochem.com,~~ which are all available electronically via the internet and which are incorporated herein by reference in their entirety. The polynucleotide sequences encoding these antibodies may be obtained from the scientific literature, from patents, and from databases such as GenBank. Alternatively, one of ordinary skill in the art may design the polynucleotide sequence to be incorporated into the genome by choosing the codons that encode for each amino acid in the desired antibody. Antibodies made by the transgenic animals of the present invention include antibodies that may be used as therapeutic reagents, for example in cancer immunotherapy against specific antigens, as diagnostic reagents and as laboratory reagents for numerous applications including immunoneutralization, radioimmunoassay, western blots, dot blots, ELISA, immunoprecipitation and immunoaffinity columns. Some of these antibodies include, but

are not limited to, antibodies which bind the following ligands: adrenomedulin, amylin, calcitonin, amyloid, calcitonin gene-related peptide, cholecystokinin, gastrin, gastric inhibitory peptide, gastrin releasing peptide, interleukin, interferon, cortistatin, somatostatin, endothelin, sarafotoxin, glucagon, glucagon-like peptide, insulin, atrial natriuretic peptide, BNP, CNP, neurokinin, substance P, leptin, neuropeptide Y, melanin concentrating hormone, melanocyte stimulating hormone, orphanin, endorphin, dynorphin, enkephalin, enkephalin, leumorphin, peptide F, PACAP, PACAP-related peptide, parathyroid hormone, urocortin, corticotrophin releasing hormone, PHM, PHI, vasoactive intestinal polypeptide, secretin, ACTH, angiotensin, angiostatin, bombesin, endostatin, bradykinin, FMRF amide, galanin, gonadotropin releasing hormone (GnRH) associated peptide, GnRH, growth hormone releasing hormone, inhibin, granulocyte-macrophage colony stimulating factor (GM-CSF), motilin, neurotensin, oxytocin, vasopressin, osteocalcin, pancreastatin, pancreatic polypeptide, peptide YY, proopiomelanocortin, transforming growth factor, vascular endothelial growth factor, vesicular monoamine transporter, vesicular acetylcholine transporter, ghrelin, NPW, NPB, C3d, prokinetican, thyroid stimulating hormone, luteinizing hormone, follicle stimulating hormone, prolactin, growth hormone, beta-lipotropin, melatonin, kallikriens, kinins, prostaglandins, erythropoietin, p146 (SEQ ID NO:18 amino acid sequence, SEQ ID NO:19, nucleotide sequence), estrogen, testosterone, corticosteroids, mineralocorticoids, thyroid hormone, thymic hormones, connective tissue proteins, nuclear proteins, actin, avidin, activin, agrin, albumin, and prohormones, propeptides, splice variants, fragments and analogs thereof.

Please replace the third full paragraph on page 31 with the following amended paragraph.

A non-limiting list of the peptides and proteins that may be made may be made through the use of the present invention is provided in product catalogs (electronically available over the internet) of companies such as Phoenix Pharmaceuticals, Inc. (~~www.phoenixpeptide.com;~~ 530 Harbor Boulevard, [[•]] Belmont, CA), Peninsula Labs (San Carlos, CA), SIGMA[[,]] (St.Louis, MO), ~~www.sigma-aldrich.com,~~ Cappel ICN, (Irvine, California), ~~www.icnbiomed.com,~~ and Calbiochem[[,]] (La Jolla, California), ~~www.calbiochem.com~~. The polynucleotide sequences encoding these proteins and peptides of interest may be obtained from the scientific literature, from patents, and from databases such as GenBank. Alternatively, one of ordinary skill in the art may design the

polynucleotide sequence to be incorporated into the genome by choosing the codons that encode for each amino acid in the desired protein or peptide.

Please replace the fifth full paragraph on page 58 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for the transposase, modified from Tn10 (GenBank accession J01829) by optimizing codons for stability of the transposase mRNA and for the expression of protein. More specifically, in each of the codons for the first ten amino acids of the transposase, G or C was changed to A or T when such a substitution would not alter the amino acid that was encoded.

Please replace the fifth full paragraph on page 60 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for the transposase, modified from Tn10 (GenBank accession J01829) by optimizing codons as discussed above.

Please replace the seventh full paragraph of Example 3 on page 61 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for the transposase, modified from Tn10 (GenBank accession J01829) by optimizing codons as discussed above.

Please replace the seventh full paragraph of Example 4 on page 63 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for the transposase, modified from Tn10 (GenBank accession J01829) by optimizing codons as discussed above.

Please replace the fourth full paragraph of Example 10 on page 72 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for a transposase, modified from Tn10 (GenBank accession number J01829).

Please replace the fourth full paragraph of Example 11 on page 73 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for a transposase, modified from Tn10 (GenBank accession number J01829).

Please replace the fourth full paragraph of Example 12 on page 75 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for a transposase, modified from Tn10 (GenBank accession number J01829).

Please replace the fourth full paragraph of Example 13 on page 76 with the following amended paragraph.

Base pairs 1780-1785 are the Kozak sequence of SEQ ID NO:13, and base pairs [[1780 – 2987]] 1783-2987 are the coding sequence for a transposase, modified from Tn10 (GenBank accession number J01829).